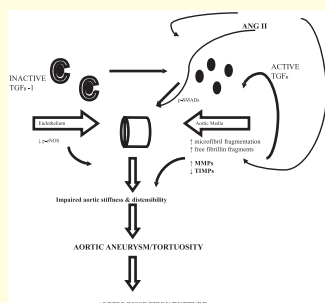




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STATE-OF-THE-ART PAPER



VIEWPOINT

JOURNAL of the AMERICAN COLLEGE of CARDIOLOGY

Inside This Issue

STATE-OF-THE-ART PAPER

Aortopathies in Congenital Heart Disease

461

Anji T. Yetman, Thomas Graham

Yetman and Graham review the literature regarding the incidence, biochemical pathways, clinical outcomes, and treatment modalities for aortic root dilation in patients with congenital heart disease. Marfan syndrome is the most obvious example where a genetic defect in the production of fibrillin is associated with aortic dilation and possible rupture, but many other congenital anomalies may also be associated with aortic dilation. Fibrillin content is also reduced in both the aorta and the pulmonary artery of patients with bicuspid aortic valve. The indications for surgical correction are reviewed.

VIEWPOINT

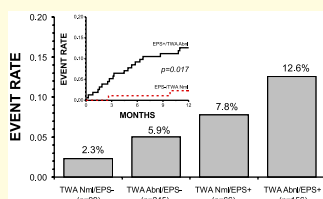
Dual RAS Blockade Improves Surrogate Outcomes, But May Worsen Hard End Points

468

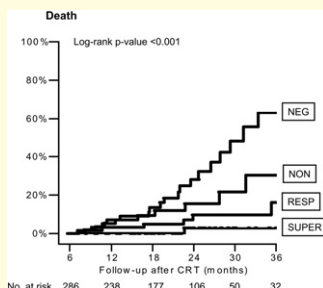
Franz H. Messerli

Messerli reviews the data on the efficacy of dual renin-angiotensin system (RAS) blockade with both an angiotensin-converting enzyme inhibitor and an angiotensin receptor blocker. Dual RAS blockade results in small reductions in blood pressure and albuminuria, and reduced hospitalizations in patients with systolic dysfunction. However, the recent larger and longer-lasting ONTARGET (Renal Outcomes With Telmisartan, Ramipril, or Both, in People at High Vascular Risk) trial found that dual RAS blockade was associated with an increased need of dialysis. A meta-analysis of dual RAS blockade for heart failure found higher rates of hypotension and worsened renal function with combination therapy and no evidence of a mortality benefit. Messerli concludes that dual RAS blockade should not be used unless long-term studies show clear reductions in hard end points.

CLINICAL RESEARCH



Editorial Comment
Gregory K. Feld and Paul Clopton,
p. 480



CLINICAL TRIAL

T-Wave Alternans Compared With EPS for Risk Prediction in ICD Patients

471

Otto Costantini, Stefan H. Hohnloser, Malcolm M. Kirk, Bruce B. Lerman, James H. Baker II, Barathi Sethuraman, Mary M. Dettmer, David S. Rosenbaum, for the ABCD Trial Investigators

The ABCD (Alternans Before Cardioverter Defibrillator) trial mandated that patients with an ischemic cardiomyopathy and nonsustained ventricular tachycardia on Holter recording undergo microvolt T-wave alternans (MTWA) testing and electrophysiologic study (EPS) prior to implantable cardioverter-defibrillator (ICD) insertion. The primary end point was appropriate ICD discharge or sudden death at 1 year. The event rate in patients with 2 normal tests was approximately 3-fold lower than in patients with 1 abnormal test and approximately 6-fold lower than in patients with 2 abnormal tests. The positive and negative predictive values of MTWA and EPS were similar. Strategies employing MTWA, EPS, or both may identify which patients are least likely to benefit from ICD insertion.

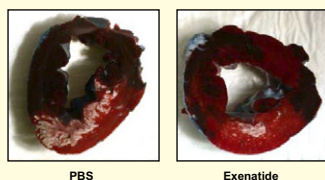
CARDIAC RESYNCHRONIZATION THERAPY

Clinical Benefit of CRT Predicted by the Magnitude of the Reduction in LVESV

483

Claudia Ypenburg, Rutger J. van Bommel, C. Jan Willem Borleffs, Gabe B. Bleeker, Eric Boersma, Martin J. Schalij, Jeroen J. Bax

Ypenburg and colleagues followed more than 300 patients who underwent cardiac resynchronization therapy (CRT) to study the relationship between left ventricular (LV) remodeling, defined as the decrease in left ventricular end-systolic volume (LVESV), and clinical outcomes. Twenty-two percent of patients were classified as super-responders (a decrease in LVESV >30%), 35% as responders (a decrease in LVESV of 15% to 29%), 21% as nonresponders (a decrease in LVESV of 0% to 14%), and 22% as negative-responders (an increase in LVESV). Clinical outcomes confirmed that the extent of LV remodeling was related to clinical outcomes including mortality and hospitalization. The extent of LV reverse remodeling at 6 months is predictive of long-term outcome in CRT patients.

PRE-CLINICAL
RESEARCH

Editorial Comment
Ian G. Webb, Rupert Williams, and
Michael S. Marber, p. 511

MEETING
HIGHLIGHTS

(continued)

A-26

PRE-CLINICAL RESEARCH

Aortic Valve Cells Have Pro-Osteogenic Phenotype That Increases Calcification 491

Xiaoping Yang, David A. Fullerton, Xin Su, Lihua Ao, Joseph C. Cleveland, Jr, Xianzhong Meng

Yang and colleagues isolated interstitial cells from both the aortic valve and the pulmonic valve in explanted hearts. Aortic valve interstitial cells (AVICs) express higher levels of toll-like receptor (TLR)2 and TLR4 than pulmonary valve interstitial cells (PVICs) isolated from the same human heart. Stimulating TLR2 or TLR4 promoted greater expression of pro-inflammatory and pro-osteogenic mediators in AVICs than in PVICs. AVICs from stenotic valves had higher levels of TLR2 and TLR4 than AVICs from normal valves. These results suggest that TLR2 and TLR4 may play an important role in aortic valve calcification and subsequent stenosis.

PRE-CLINICAL RESEARCH

Exenatide Reduces Ischemia Reperfusion Injury in a Pig Model 501

Leo Timmers, José P. S. Henriques, Dominique P. V. de Kleijn, J. Hans DeVries, Hans Kemperman, Paul Steendijk, Cees W. J. Verlaan, Marjolein Kerver, Jan J. Piek, Pieter A. Doevendans, Gerard Pasterkamp, Imo E. Hofer

Exenatide is a small glucagon-like peptide (GLP-1) analogue, originally derived from the saliva of the gila monster, that may reduce apoptosis and reperfusion injury. Timmers and colleagues randomized pigs to exenatide or placebo following 75 min of coronary artery ligation and prior to subsequent reperfusion. Exenatide reduced the infarct size from 54% to 33% of the area at risk and prevented deterioration of systolic and diastolic cardiac function. This was associated with reduced cellular apoptosis. These data identify exenatide as a potentially effective addition to reperfusion therapy in patients with acute myocardial infarction.

MEETING HIGHLIGHTS

Highlights From the 2008 Heart Failure Society of America Meeting 514

Mandeep R. Mehra, Howard A. Rockman, Barry H. Greenberg

Mehra and colleagues report the highlights from the 2008 Scientific Sessions of the Heart Failure Society of America, which was held in September 2008. Highlights included a session focused on the relationship of environmental factors to heart failure, including increased rates of obesity in urban population. Several studies that were presented as late breaking clinical trials are also summarized. The MOMENTUM (Orqis Medical Cancion System for the Enhanced Treatment of Heart Failure Unresponsive to Medical Therapy) trial identified a group of patients who may benefit from a percutaneously placed aortic flow assist device, and other trials suggested that the efficacy of long-acting carvedilol did not differ from immediate release and that sertraline appears safe in patients with heart failure. The development of guidelines for heart failure management is also discussed.